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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,683	11/15/2001	David Botstein	P2730P1C32	4971

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/997,683	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/15/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after at least three rejections and the filing of a notice of appeal. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

Claims 119-123 are under examination in the instant office action.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-123 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility.

Claims 119-123 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific, and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

A portion of the basis for these rejections is withdrawn. Specifically, the examiner no longer asserts that **mRNA levels** are not predictive of polypeptide levels. Therefore, the following references are no longer being relied upon to support the rejections: Chen et al., Hu et al., LaBaer, Haynes et al., Gygi et al., Lian et al., Fessler et al., Nagaraja et al., Waghray et al., Sagnaliev et al., Lilley et al., Wildsmith et al., King et al., Bork et al., Celis et al., and Madoz-Gurpide et al. The following references cited and discussed by Applicant pertaining to the mRNA/polypeptide correlation issue will no longer be addressed: Futcher et al., Alberts and Lewin, Meric et al., Zhigang et al., Wang et al., Munaut et al. The basis of the maintained rejections is solely that **gene amplification levels** are not predictive of mRNA or polypeptide levels.

In the interest of clarity, the basis of the maintained rejections is set forth thusly:

The claims are directed to antibodies that bind specifically to polypeptides comprising the amino acid sequence of SEQ ID NO: 351, wherein the nucleic acid encoding said polypeptide is amplified in lung cell carcinomas. The claims do not require that the cognate polypeptides be overexpressed in any tumor, or have any biological activity. Claims are also presented to humanized antibodies and monoclonal antibodies. The specification discloses the antibody that binds the polypeptide of SEQ ID NO: 351, also known as PRO1153. Applicants have gone on the record as relying upon the gene amplification assay as providing utility and enablement for the disclosed cognate polypeptides. See Remarks (received 11 July 2007), p. 2, beginning of Arguments.

At pages 549-555 of the specification, Example 170 discloses a gene amplification assay

in which genomic DNA encoding PRO1153 had a ΔCt value of at least 1.0 for two out of fourteen lung tumor samples when compared to a pooled control of blood DNA from several healthy volunteers. Example 170 asserts that gene amplification is associated with overexpression of the gene product (i.e., the polypeptide), indicating that the polypeptides are useful targets for therapeutic intervention in cancer and diagnostic determination of the presence of cancer (p. 539, lines 21-24). At page 548, ΔCt is defined as the threshold PCR cycle, or the cycle at which the reporter signal accumulates above the background level of fluorescence. The specification further indicates that ΔCt is used as "a quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results." It is noted that at page 548, it is stated that samples were used if their values were within 1 Ct of the 'normal standard'. It is further noted that the ΔCt values at pages 550-554 are expressed (a) with values to one one-hundredth of a unit (e.g. 1.29), and (b) that very few values were obtained that were at least 2.

Firstly, there are several problems with the data provided in this example. Only two out of the fourteen lung cancer samples tested positive. Therefore, if a sample were taken from an individual with lung cancer for diagnosis, ***it is more likely than not that this assay would yield a false negative result***. Furthermore, the art recognizes that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy **before** the epithelial cells turn cancerous. See Hittelman (2001, Ann. N. Y. Acad. Sci. 952: 1-12, of record, especially p. 4, Figure 4) who teach that damaged, precancerous lung epithelium is often aneuploid. The gene amplification assay in the instant specification does not provide a comparison between the lung tumor samples and normal lung epithelium and does not

correct for aneuploidy. Thus it is not clear that PRO1153 is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium. One skilled in the art would not conclude that PRO1153 is a diagnostic probe for lung cancer unless it is clear that PRO1153 is amplified to a clearly greater extent in true lung tumor tissue relative to non-cancerous lung epithelium.

Secondly, even if the data had been corrected for aneuploidy and a proper control had been used, and even if a majority of lung tumor samples had tested positive, the data have no bearing on the utility of the claimed PRO1153 *antibodies*. The usefulness of the claimed antibodies depends on whether they are useful to detect their cognate polypeptides. However, in order for PRO1153 polypeptides to be overexpressed in tumors, amplified genomic DNA would have to correlate with increased mRNA levels and increased polypeptide levels. No data regarding PRO1153 mRNA or PRO1153 polypeptide levels in lung tumors have been brought forth on the record. The art discloses that a correlation between genomic DNA levels and mRNA levels cannot be presumed, nor can any correlation between genomic DNA levels and polypeptide levels. A specific example of the lack of correlation between genomic DNA amplification and increased mRNA expression is provided by Pennica et al. (1998, PNAS USA 95:14717-14722, of record), who disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient." (p. 14722, second paragraph of left column; pp. 14720-14721)

Another specific example is provided by Konopka et al. (Proc. Natl. Acad. Sci. (1986) 83:4049-4052), who state: "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template" (see abstract).

The *general* concept of gene amplification's lack of correlation with mRNA/protein overexpression in cancer tissue is addressed by Sen (2000, Curr. Opin. Oncol. 12:82-88, of record). Specifically, Sen teaches that cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes. A slight amplification of a gene does not necessarily correlate with overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. Hittelman also speaks to this issue. Again, the data in the specification were not corrected for such aneuploidy events. Furthermore, Godbout et al. (1998, J. Biol. Chem. 273(33): 21161-21168, of record) speak to general lack of correlation between gene amplification and mRNA/protein overexpression. The abstract of Godbout teaches "The DEAD box gene, DDX1, is a putative RNA helicase that is co-amplified with MYCN in a subset of retinoblastoma (RB) and neuroblastoma (NB) tumors and cell lines. ***Although gene amplification usually involves hundreds to thousands of kilobase pairs of DNA, a number of studies suggest that co-amplified genes are only overexpressed if they provide a selective advantage to the cells in which they are amplified.***" (Emphasis added). The protein encoded by the DDX gene *had been characterized* as being a putative RNA helicase, a type of enzyme that *would be expected to confer a selective advantage* to the cells in which it (the DDX gene) was amplified. On page 21167, right column, first full paragraph, Godbout et al. state "***It is generally accepted that co-amplified genes are not over-expressed unless they provide a***

selective growth advantage to the cell (48, 49). For example, although ERBA is closely linked to ERBB2 in breast cancer and both genes are commonly amplified in these tumors, ERBA is not overexpressed (48). Similarly, three genes mapping to 12q13-14 (CDK4, SAS and MDM2) are overexpressed in a high percentage of malignant gliomas showing amplification of this chromosomal region, while other genes mapping to this region (GADD153, GL1, and A2MR) are rarely overexpressed in gene-amplified malignant gliomas (50, 51). The first three genes are probably the main targets of the amplification process, while the latter three genes are probably incidentally included in the amplicons." (Emphasis added). There is no evidence in the instant application that PRO1153 confers any growth advantage to a cell, and thus it cannot be presumed that the protein is overexpressed because the genomic DNA including the gene being studied gene is amplified.

An additional reference that provides evidence that gene amplification does not generally lead to increased transcript is Li et al. (2006, Oncogene, Vol. 25, pages 2628-2635, of record). Li et al. used a functional approach that integrated simultaneous genomic and transcript microarray, proteomics, and tissue microarray analyses to directly identify putative oncogenes in lung adenocarcinoma. On page 2633, right column, Li et al. state: ***"In our study, 68.8% of the genes showing over-representation in the genome did not show elevated transcript levels***, implying that at least some of these genes are 'passenger' genes that are concurrently amplified because of their location with respect to amplicons but *lack biological relevance in terms of the development of lung adenocarcinoma.*" Since more than half of the amplified genes were not overexpressed, Li et al. constitutes strong evidence that ***it is more likely than not that gene amplification does NOT correlate with increased protein levels***, absent evidence that the protein

has biological relevance in cancer. There is no such evidence for PRO1153.

Therefore, data pertaining to PRO1153 genomic DNA do not indicate anything significant regarding the claimed PRO1153 antibodies or to the polypeptides to which they bind. The data do not support the specification's assertion that PRO1153 antibodies can be used as a cancer diagnostic agent. Significant further research would have been required of the skilled artisan to reasonably confirm that the claimed PRO1153 polypeptides are overexpressed in any cancer to the extent that they could be used as cancer diagnostic agents; thus the asserted utility is not substantial. In the absence of information regarding whether or not PRO1153 polypeptide levels are also different between specific cancerous and normal tissues, the proposed use of the PRO1153 **antibodies** as diagnostic markers and therapeutic tools are simply starting points for further research and investigation into potential practical uses of the antibodies. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), the Court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

In view of the preponderance of evidence supporting the rejections (Pennica et al., Konopka et al., Sen, Hittelman, Godbout et al., and Li et al., all of which are of record and have been previously discussed), the rejections are properly maintained.

Applicants' arguments pertaining to the remaining issues (Remarks, 11 July 2007) have been fully considered but are not found to be persuasive for the following reasons. Applicants begin with a review of the legal standard for utility, with which the examiner takes no issue.

Beginning at p. 8 of the Response, Applicants refer to the Polakis declaration as establishing that an amplification of at least 2-fold is significant and indicative of a cancer diagnostic marker. The Polakis declaration under 37 CFR 1.132 filed 16 June 2004, as well as the Ashkenazi declaration filed on the same date are insufficient to overcome the rejection of claims 119-123 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action for the following reasons. In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). In the instant situation, the nature of the fact sought to be established is whether or not a 2.01 to 2.52-fold amplification of the gene encoding PRO1153 in two lung tumors is significant. The significance can be questioned based on the absence of factual support for the expert's opinion. In the instant case, the facts are that twelve of the fourteen lung tumor samples did not show an amplification of the gene encoding PRO1153, and the control used was not a matched non-tumor lung sample but rather was a pooled DNA sample from blood of healthy subjects. The art uses matched tissue samples (see Pennica et al., Konopka et al.). This art, as well as the Sen, Hittelman, Godbout et al., and Li et al. references cited above, constitute strong opposing evidence as to whether or not the claimed polypeptides have utility and enablement based on a presumption of overexpression in view of gene amplification data. Finally, while the Goddard declaration speaks to the utility and

enablement of amplified genes, it does not speak to whether or not the encoded proteins are also found at increased levels in cancerous tissues. Since the claims under examination are directed to antibodies against PRO polypeptides, not genes, this question is critical.

Applicants argue that the PRO1153 gene is an important diagnostic marker to identify malignant lung carcinomas even when the lung malignancy associated with the PRO1153 molecule is a rare occurrence. Applicants urge that evidence has been provided that the PRO1153 polypeptide is significantly amplified in certain types of lung carcinoma tumors and is therefore a valuable diagnostic marker for identifying certain types of lung carcinomas. This has been fully considered but is not found to be persuasive. Firstly, Applicants are incorrect with regard to the facts. It is important to clarify that no evidence has been brought forward to establish that the PRO1153 **polypeptide** is amplified in any lung tumors. The only evidence directly related to PRO1153 is found in Example 170 of the specification, which indicates that PRO1153 **gene** is amplified in two out of fourteen lung tumors as compared to a pooled blood DNA sample. Even if it were determined that the antibodies were diagnostic for cancer, it is more likely than not that a false negative result would be obtained. Secondly, the PRO1153 gene was not amplified in twelve out of fourteen lung tumor samples, thus establishing that it is more likely than not that a lung sample from a patient suspected of having lung cancer will yield a false negative result in the disclosed assay. While it is true that markers for rare cancers are valuable, they are only valuable if the rare tumor is adequately described and distinguished from other tumors. Applicants stated in the arguments that PRO1153 is amplified in "certain types of lung carcinoma tumors." However, the specification and evidence of record do not establish which certain types these lung carcinomas are. Additionally, even if it could be established that

PRO1153 gene is significantly amplified in lung carcinomas, it does not follow that PRO1153 polypeptide would also be over-expressed and thus useful as a cancer diagnostic molecule, for reasons discussed extensively on the record.

Applicants point to the statement in Example 170 that gene amplification is associated with overexpression of the gene product, thus allegedly indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers and for the diagnostic determination of the presence of those cancers. This has been fully considered but is not found to be persuasive. Substantial evidence has been brought forth to establish that it is more likely than not that gene amplification is not associated with overexpression of the disclosed protein to which the claimed antibody binds.

Applicant relies on Orntoft et al., Hyman et al., and Pollack et al. as evidence that gene amplification increases mRNA expression in general. This has been fully considered but is not found to be persuasive. Orntoft et al. used the CGH method to look at increased DNA content over large regions of chromosomes and comparing that to mRNA and polypeptide levels from the chromosomal region. However, Orntoft et al. do not look at gene amplification, mRNA levels and polypeptide levels from a single gene at a time. The instant specification reports data regarding amplification of individual genes, which may or may not be in a chromosomal region which is highly amplified. Orntoft et al. concentrated on regions of chromosomes with strong gains of chromosomal material containing clusters of genes (p. 40). This analysis was not done for PRO1153 in the instant specification. That is, it is not clear whether or not PRO1153 is in a gene cluster in a region of a chromosome that is highly amplified. Therefore, Orntoft et al. does not support utility and enablement of the claimed polypeptides. Hyman et al. used the same

CGH approach in their research. Less than half (44%) of highly amplified genes showed mRNA overexpression (abstract). Polypeptide levels were not investigated. Therefore, Hyman et al. also do not support utility of the claimed polypeptides. Pollack et al. also used CGH technology, concentrating on large chromosome regions showing high amplification (p. 12965). Pollack et al. did not investigate polypeptide levels. Therefore, Pollack et al. also do not support the asserted utility of the claimed invention. Importantly, none of the three papers reported that the research was relevant to identifying probes that can be used as cancer diagnostics. The three papers state that the research was relevant to the development of **potential** cancer therapeutics, but also clearly imply that much further research was needed before such therapeutics were in readily available form. Accordingly, the specification's assertions that the claimed PRO1153 antibodies have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

Applicant refers to the Polakis Declaration of 16 June 2004. The Polakis Declaration under 37 CFR 1.132 filed 16 June 2004 is insufficient to overcome the rejection of claims 119-123 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action because the declarations focus on the question of whether or not mRNA levels are predictive of protein levels. As explained above, the examiner is no longer arguing this point. Since the Polakis declaration does not address the question of whether or not amplified genomic DNA is predictive of increased polypeptide levels, they are no longer considered pertinent to the rejection.

The specification provides no assertion that the claimed PRO1153 antibodies are useful in tumor categorization, nor does it provide guidance regarding what treatment modalities should be

selected by a physician depending upon whether or not a tumor overexpresses PRO1153. No evidence has been brought forth on the record as to whether or not the cognate polypeptide is overexpressed in lung tumors. Furthermore, the specification does not assert a utility for the claimed polypeptides based on the possibility that the PRO1153 polypeptide is not overexpressed in lung cancer tissue.

Beginning at p. 5 of the Remarks, Applicants discuss the Orntoft et al. publication. Specifically, Applicants urge that Orntoft et al. looked at the correlation of mRNA levels and protein expression for individual genes. Applicants argue that Orntoft et al. find that there is a highly significant correlation between mRNA and protein alterations. Applicant argues that a correlation in 39 out of 40 gene examined supports their position that mRNA correlates with protein levels. This has been fully considered but is not found to be persuasive. Firstly, the rejection is no longer based on the issue of whether or not mRNA levels are predictive of protein levels. Therefore, these findings of Orntoft et al. are no longer relevant to the rejection. Regarding the correlation of gene amplification with increased protein levels, Orntoft et al. could only compare the levels of about 40 well-resolved and focused *abundant* proteins." (See abstract.) Moreover, Orntoft et al. only concentrated on regions of chromosomes with strong gains of chromosomal material containing clusters of genes (pg 40). This analysis was not done for PRO1153 in the instant specification. That is, it is not clear whether or not PRO1153 is in a gene cluster in a region of a chromosome that is highly amplified. Therefore, Orntoft et al.'s results cannot be extended to the instant gene and protein.

At p. 9, Applicants conclude that, based on the asserted utility for PRO1153 in the diagnosis of selected lung carcinomas, the reduction to practice of the PRO1153 protein

sequence, the disclosure of methods for making polypeptides comprising PRO1153 and antibodies that bind PRO1153, and example 170 regarding the gene amplification assay, one skilled in the art would know exactly how to make and use the claimed antibodies for diagnosis of lung carcinoma without undue experimentation. Applicants urge that, in general, DNA amplification correlates with increased expression of the encoded protein. Applicants argue that the specification shows significant amplification in two different lung primary tumors, evidence in the form of publications has been submitted to establish that a general DNA/mRNA/protein correlation exists, and declarations from experts have been provided to further support Applicants' position. Applicants conclude that the utility of the claimed PRO1153 antibody has been achieved. This has been fully considered but is not found to be persuasive for the following reasons. Regarding the gene amplification assay itself, it is noted that PRO1153 gene was not amplified in twelve out of fourteen lung carcinoma samples. Therefore, PRO1153 it is more likely than not that a lung carcinoma sample will not have amplified PRO1153. Also, the assay did not correct for aneuploidy, which is a common feature of non-cancerous, damaged lung epithelium (evidenced by Hittelman). Contrary to Applicants' assertions, the state of the art indicates that gene amplification is not generally associated with overexpression of the encoded gene product, as evidenced by Sen, Pennica et al., Konopka et al., Hanna and Mornin, Godbout et al., Hyman et al., and Li et al. Since significant further research would have been required of the skilled artisan to reasonably confirm that the claimed PRO1153 polypeptides are overexpressed in any cancer to the extent that they could be used as cancer diagnostic agents, the asserted utility is not substantial. In the absence of information regarding whether or not PRO1153 polypeptide levels are also different between specific cancerous and normal tissues,

the proposed use of the PRO1153 **antibodies** as diagnostic markers and therapeutic tools are simply starting points for further research and investigation into potential practical uses of the antibodies.

35 U.S.C. 101, Product of Nature

Claim 119 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claim reads on a product of nature in that the claimed antibody is not "isolated." For example, the claims encompass polyclonal sera that has not been removed from the human or animal. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty,* 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105.

Conclusion

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
19 September 2007

Eileen B. O'Hara
EILEEN B. O'HARA
PRIMARY EXAMINER